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Selective Iron-Catalyzed Deaminative Hydrogenation of Amides

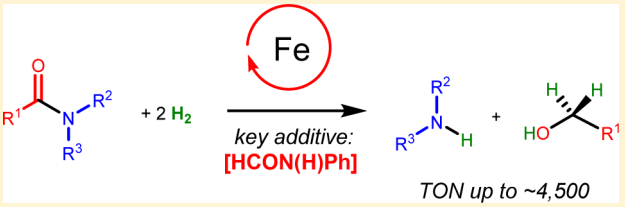
Upul Jayarathne,[†] Yuanyuan Zhang,[†] Nilay Hazari,[‡] and Wesley H. Bernskoetter*[,†]

[†]Department of Chemistry, University of Missouri, Columbia, Missouri 65211, United States

[‡]Department of Chemistry, Yale University, New Haven, Connecticut 06520, United States

Supporting Information

ABSTRACT: The five-coordinate iron(II) hydride complex (^{iPr}PNP)Fe(H)CO (^{iPr}PNP = N[$CH_2CH_2(P^iPr_2)]_2$) was found to selectively catalyze deaminative hydrogenation of amides to the corresponding amines and primary alcohols. It is one of the most active amide hydrogenation catalysts reported to date, with turnover numbers (TONs) in excess of 1000 observed for multiple substrates and TONs greater than 4000 obtained for activated formanilides. The amide C−N cleavage reactions occur with a preference for electron-withdrawing substituents and with greater activity for formamides compared with acetamides and benzamides. Stoichiometric reactions between (^{iPr}PNP)Fe(H)CO and formanilide afforded the new iron(II) complex (^{iPr}PN^{H}P)Fe(H)CO(N(Ph)HCO) resulting from N−H addition across the Fe−N bond. Complexes of this type were identified as the resting state during catalytic hydrogenation reactions containing secondary amides. Addition of a Lewis acid cocatalyst provided further enhancement of the productivity of catalytic amide hydrogenations.



INTRODUCTION

Amides are among the most pervasive functional groups in naturally occurring molecules.[1] These relatively unreactive carboxylic acid derivatives have diverse roles in chemistry ranging from the structural backbone in peptide linkages to small-molecule therapeutic agents.[2] Synthetic chemists have long sought efficient and selective catalytic methods to reduce amides via hydrogenation as an alternative to contemporary methods for reduction that rely heavily on waste-generating stoichiometric reagents.[3] Traditionally, efforts to develop amide hydrogenation catalysts have focused on homogeneous ruthenium systems, and there are now multiple examples of catalysts that selectively reduce amides via C−N bond cleavage (deaminative hydrogenation) or C−O bond cleavage (deoxygenative hydrogenation) (Figure 1). Both reduction pathways

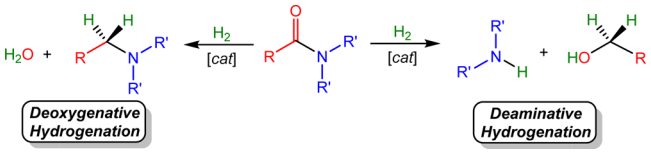


Figure 1. Divergent selectivity for the hydrogenation of amides.

are potentially useful, with the difference in selectivity related to the mechanism through which a common intermediate hemiaminal species reacts.[4] While several highly active heterogeneous catalysts for amide hydrogenation have been recently reported, their poor selectivity, including reduction of ancillary aromatic rings,[5] has led to increased research effort to develop improved homogeneous catalysts.[6,7] Bergens and co-workers reported one of the most active catalytic systems for deaminative hydrogenation, achieving a turnover number (TON) of 1000 using a combination of [Ru(η^3-C_3H_5)(Ph_2P-$(CH_2)_2NH_2)_2$]BF_4 (**A**) and 2 equiv of $NaBH_4$ to reduce *N*,*N*-diphenylacetamide (50 atm, 100 °C, 24 h) (Figure 2).[8] In fact, nearly all of the previously reported ruthenium catalysts for deaminative hydrogenation require the addition of exogenous base, with most of the other systems also failing to demonstrate TONs of >500. The exceptions to this trend are the PNN-pincer ruthenium catalysts **B** and **C** (Figure 3) described by Milstein[9] and Beller[10] that do not require a base. Catalyst **B** hydrogenates a range of amide substrates, with TONs limited to ca. 100 (10 atm, 110 °C, 48 h),[9] while catalyst **C** is even more active, achieving TONs near 500 for multiple amides (30 atm, 120 °C, 18 h).[10]

While state-of-the-art catalysts for amide hydrogenation are currently based on ruthenium, developing more active catalysts using less expensive and toxic metals would greatly enhance the prospects for the large-scale utilization of deaminative hydrogenation methods. To date, homogeneous base-metal catalysts for amide hydrogenation are exceedingly rare.[11] Milstein and co-workers recently reported the first such species, the pyridyl-based iron pincer complex [C_5H_3N-2,6-($CH_2P^iPr_2)_2$]Fe(H)Br-(CO) (**D**), which, when combined with exogenous base, hydrogenated N-substituted 2,2,2-trifluoroacetamides to give the corresponding amines and trifluoroethanol, in some cases with high conversions (99%) and TONs of up to 50 (60 atm, 140 °C, 12−36 h) (Figure 4).[11a] Unfortunately, the hydrogenation was limited to only CF_3-activated amides, and no reaction was observed with more common substrates such as *N*-phenylacetamide and *N*-phenylbenzamide. Our own laboratories, along with other investigators, have developed related

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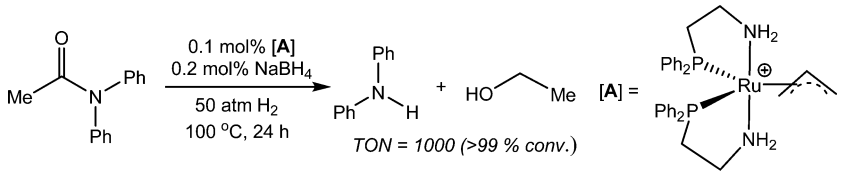
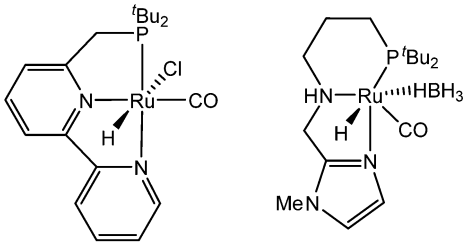


Figure 2. Ruthenium-catalyzed hydrogenation of *N*,*N*-diphenylacetamide described by Bergens and co-workers.[8]



B **C**

Figure 3. Ruthenium PNN-pincer catalysts for deaminative amide hydrogenation.

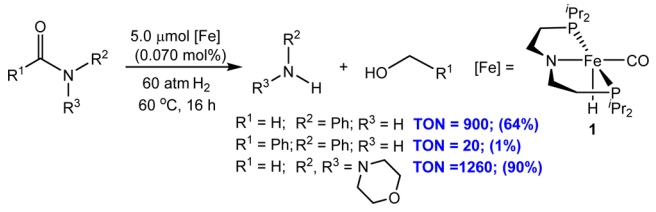


Figure 5. Initial studies of amide hydrogenation catalyzed by **1**.

pincer-supported iron catalysts for a variety of hydrogenation and dehydrogenation reactions.[12] The five-coordinate iron(II) complex (^{R}PNP)Fe(H)CO (^{R}PNP = N[$CH_2CH_2(PR_2)$]$_2$, R = ^{i}Pr, Cy) has proven particularly effective at hydrogenating substrates such as esters, olefins, nitrogen heterocycles, and CO_2.[13] Herein we report the application of [(^{R}PNP)Fe] catalysts in the selective base-free hydrogenation of a range of secondary and tertiary amides. The catalytic TONs for many of these amide substrates surpass even those of precious-metal catalysts. From a fundamental perspective, the addition of Lewis acid salts and small amounts of a secondary amide result in significantly enhanced activity for challenging substrates.

RESULTS AND DISCUSSION

Our investigation into iron-catalyzed amide hydrogenation began with experiments using (^{iPr}PNP)Fe(H)CO (**1**) as the catalyst for the reduction of formanilide, *N*-phenylbenzamide, and 4-formylmorpholine (Figure 5). Despite the use of relatively mild conditions (60 atm, 60 °C, 16 h), the initial catalytic results were highly promising. Catalyst **1** hydrogenated both formamide substrates with TONs comparable to or slightly higher than those of the most active ruthenium catalysts reported to date and with essentially complete selectivity for methanol and the corresponding amines.[14] These observations suggested that unprecedented catalytic activity may be possible with further optimization and mechanistic insight. Even the small TON of 20 for *N*-phenylbenzamide was noteworthy given the inability of Milstein's iron catalyst **D** to reduce this substrate. During the course of the investigations described herein, two related iron hydridoborohydride carbonyl pre-catalysts,{HN[$CH_2CH_2(PR_2)$]$_2$}Fe(H)CO(η^1-BH_4) (R = Et, Cy), were reported by Langer and Sanford, respectively.[11b,c] As part of a study of ester hydrogenation, the Et_2P-substituted pincer complex was reported to hydrogenate a small group of amides, with a comparable TON of 23 for *N*-phenylbenzamide (50 atm, 70 °C, 24 h). Oddly, the scope and general activity of this precatalyst are considerably weaker than observed here, possibly as a result of small differences in the ancillary ligand or precatalyst structure (vide infra).[11b] The Cy_2P-substituted analogue exhibited a comparable TON of 25 for *N*-phenylbenzamide (50 atm, 130 °C, 3 h) but was successful at hydrogenating a broader range of 2° and 3° amides than the Et_2P-substituted congener, with TONs of 25−300 commonly observed (a notable TON of 1080 was achieved for dimethylformamide). However, in catalysis using {HN[$CH_2CH_2(PCy_2)$]$_2$}Fe(H)CO(η^1-BH_4) an exogenous base was required to obtain the best performance.

Given the high preliminary TONs in the reduction of 4-formylmorpholine and formanilide using **1**, we employed these amides to screen different conditions for hydrogenation. Altering the reaction conditions for the hydrogenation of 4-formylmorpholine in Figure 5 from 60 atm H_2 to 30 atm lowered the TON to 1090. However, this drop in activity could be recovered by raising the temperature to 100 °C, affording a TON of >1390 (~99% conv.) at 30 atm. Periodic sampling of this reaction indicated complete conversion was achieved after only 4 h, providing a new set of standard reaction conditions of 30 atm H_2 at 100 °C over 4 h. Following this optimization, the influence of the solvent was examined using a 1.25 μmol (0.018 mol %, TON_{max} = 5600) catalyst loading (Table 1). In these reactions, solid formanilide was preferred over liquid 4-formylmorpholine as the substrate because of the relative ease of purifying, drying, and handling the multigram quantities required to complete these catalytic trials. Aside from a notable

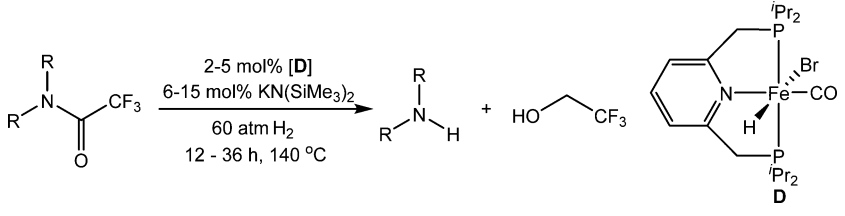


Figure 4. First iron-catalyzed hydrogenation of trifluoroacetamides reported by Milstein and co-workers.

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Table 1. Solvent Screening for Formanilide Hydrogenation Catalyzed by 1[a]

solvent	TON[b]
tetrahydrofuran	3240
1,4-dioxane	2300
acetonitrile	<10
ethyl acetate	2440
toluene	2840

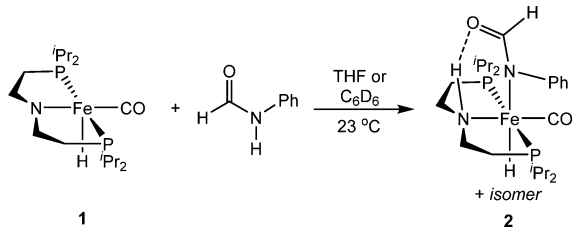
[a]Reaction conditions: 30 atm H_2 (450 psi), 1.25 μmol of **1** (0.018 mol %), and 7 mmol of formanilide in 5 mL of solvent at 100 °C for 4 h. [b]Determined by NMR spectroscopic analysis of the product amine and residual starting material. Each entry is the average of two or more trials.

inactivity in acetonitrile, probably due to catalyst decomposition, the catalyst performed well in several polar solvents, with THF providing the highest TON of 3240. Our system is also compatible with nonpolar solvents such as toluene, although many amide substrates have limited solubility in these media.

The substrate scope of amide hydrogenation catalyzed by **1** was explored using conditions based on our reaction optimization (Table 2). A series of amides were hydrogenated under 30 atm H_2 at 100 °C over 4 h in THF with a 5.0 μmol loading of **1** (0.070 mol %; TON_{max} = 1400). Those substrates that achieved >90% conversion under these conditions were also tested with a 1.25 μmol (0.018 mol %; TON_{max} = 5600) loading of **1** to better ascertain the limits of the activity. The results offer several insights into trends associated with iron-catalyzed deaminative hydrogenation. Entries 1−5 indicate a moderate preference for the hydrogenation of amides bearing electron-withdrawing N-substituents, with the *p*-CF_3-substituted formanilide affording ca. 2500 additional turnovers compared with the *p*-OMe-substituted congener under low-catalyst-loading conditions. Notably, at higher catalyst loading all of the studied formanilides were fully hydrogenated to the corresponding amines and alcohols with essentially complete selectivity. Consistent with the electronic activation of the formanilides, secondary formamides were more reactive than the related tertiary formamides (entries 3, 6, and 7), with those bearing aryl groups achieving higher TONs than alkylated formamides. 4-Formylmorpholine (entry 8) is a notable exception to this trend, although the presence of a cyclic substituent differentiates it from other substrates. The general preference for deaminative hydrogenation of electron-poor substrates is also evident in the variation in catalytic performance as the amide carbonyl substituent was changed (entries 3 and 9−11). Comparison of the TONs for the CH_3- and CF_3-substituted carbonyl (entries 9 and 11) with the H-substituted formamide (entry 3) also suggests that steric factors play an important role in hydrogenation. Both of the larger amides are more challenging substrates, despite providing electronically different influences.

As noted earlier, the low loadings of **1** required that amide substrates be purified and dried prior to use in catalytic reactions. As a practical test for purity, substrates were routinely mixed with formanilide (ca 700 equiv of each with respect to **1**) and hydrogenated under the conditions used in Table 2. The hypothesis was that impurities in the new substrates would become evident from a reduction in the conversion of formanilide, which is otherwise fully hydrogenated to aniline and methanol under these conditions. During the course of these tests, a serendipitous observation was made regarding tertiary formamide substrates. For example, when *N*-methylformanilide was used as the substrate in the presence of formanilide, both compounds were completely hydrogenated, equivalent to a TON of 700 for each amide; however, independent hydrogenation of *N*-methylformanilide afforded vanishingly small conversion (Table 2, entry 6). The origin of this enhancement of deaminative hydrogenation was probed by performing separate catalytic trials of *N*-methylformanilide hydrogenation with 20 equiv (with respect to **1**) of formanilide, aniline, and methanol. Hydrogenations containing aniline and/or methanol (the products of formanilide hydrogenation) afforded TONs of less than 350 (Table S3), suggesting that formanilide itself improved the conversion. Indeed, addition of 20 equiv (with respect to **1**) of formanilide to *N*-methylformanilide hydrogenation (Figure 6) increased the TON from 60 to 1300 under the conditions in Table 2. Similar activity enhancements were also observed when formanilide was spiked into other tertiary amides (vide infra).

A series of NMR experiments were performed to examine the mechanism of formanilide enhancement of amide hydrogenation. First, the stoichiometric treatment of **1** with formanilide (eq 1) resulted in a bleaching of the dark-red



(1)

solution to yellow and the observation of two new resonances in the ^{31}P NMR spectrum. These singlet peaks appeared at 96.85 and 91.14 ppm in a 1:3 ratio, suggesting two isomeric products. The corresponding ^1H NMR spectrum also held several resonances of interest, including a pair of triplet Fe−H signals at −22.82 ppm (major) and −25.98 ppm (minor). The downfield region of the NMR spectrum revealed four resonances ranging from 8 to 11 ppm assigned to the ($^{iPr}PN^HP$) N−H and formamide C−H moieties with the aid of $^1H-^{13}C$ HMQC NMR experiments. These data are consistent with formation of an iron(II) formanilide hydride carbonyl complex, ($^{iPr}PN^HP$)Fe(NPhCHO)CO(H) (**2**), produced by formal addition of the amide N−H across the Fe−N bond. The presence of two isomeric products is likely due to the formation of conformational isomers of the formanilide as a result of hindered rotation about the C−N bond. Isomers varying through different coordination sites of the formanilide, hydride, and CO ligands are also possible, though less likely given the need to partially dissociate the $^{iPr}PN^HP$ ligand in order to interchange these positions. Assignment of the formanilide complex was confirmed by single-crystal X-ray diffraction of a sample containing one isomer of **2** (Figure 7). The molecular structure of **2** exhibits a slightly distorted octahedral geometry about the iron center with the Fe(1)−N(2) formamide linkage lying opposite the Fe(1)−H(1) bond. The bound amide appears to be hydrogen-bonded to the pincer N−H bond, with a short interaction distance of 1.84 Å between O(2) and H(2). To further elucidate the details of the amide hydrogenation reaction, a pair of NMR-tube-scale catalytic reactions were monitored in situ. Two J. Young NMR tubes

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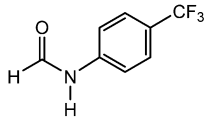
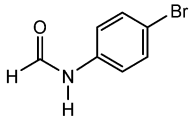
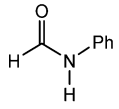
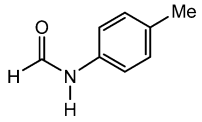
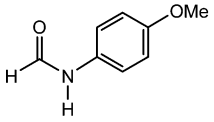
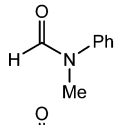
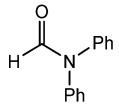
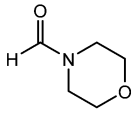
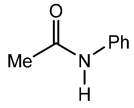
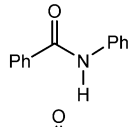
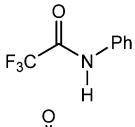
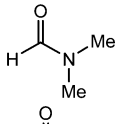
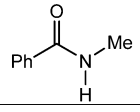
Table 2. Deaminative Hydrogenation of Amides Catalyzed by 1[a]

Entry	Substrate	0.070 mol% 1 TON (Conv.)[b]	0.018 mol% 1 TON (Conv.)[b]
1		>1390 (>99%)	4430 (79%)
2		>1390 (>99%)	3360 (60%)
3		>1390 (>99%)	3240 (58%)
4		>1390 (>99%)	2610 (47%)
5		>1390 (>99%)	1920 (34%)
6		60 (4%)	--
7		1190 (85%)	--
8		1360 (97%)	2000
9		50 (<5%)	--
10		130 (9%)	--
11		160 (11%)	--
12		No conversion	--
13		No conversion	--

[a]Reaction conditions: 30 atm H_2 (~450 psi), 5.0−1.25 μmol of **1** (0.07−0.018 mol %), and 7 mmol of amide in 5 mL of THF at 100 °C for 4 h. [b]Determined by NMR and GC analyses of the product amine or alcohol (in the case of highly volatile product amines) as well as residual starting material. Each entry is the average of two or more trials.

were charged with a benzene-d_6 solution of **1** and 4 equiv of *N*-methylformanilide. No apparent reaction between the tertiary amide and the five-coordinate iron compound was detected at ambient temperature over 1 h (Figures S5 and S6). Then

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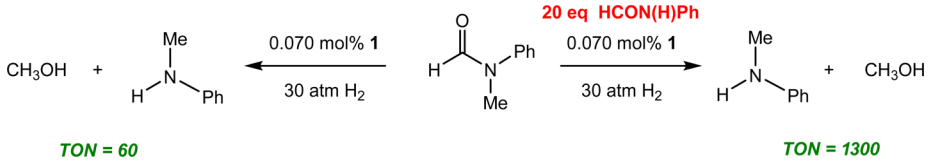


Figure 6. Influence of 2° amide addition on *N*-methylformanilide hydrogenation.

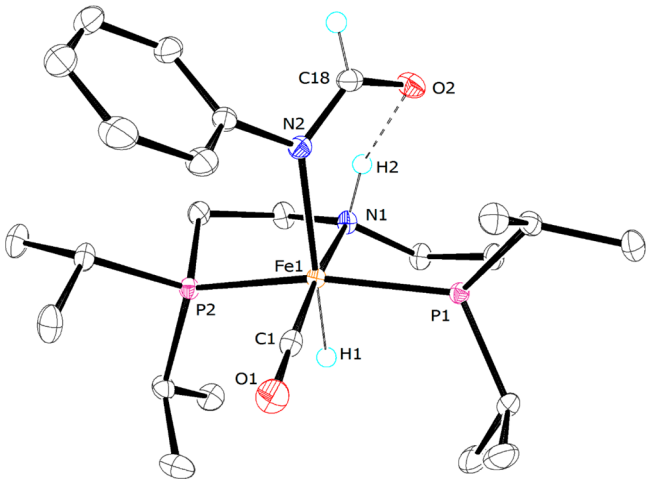
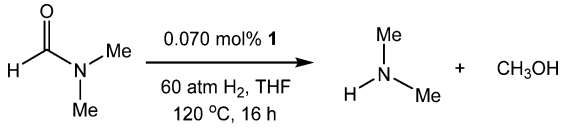


Figure 7. Molecular structure of **2** with 30% ellipsoids. Most of the hydrogen atoms have been removed for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)−P(1) 2.2190(3), Fe(1)−P(2) 2.2042(3), Fe(1)−N(1) 2.0855(8), Fe(1)−C(1) 1.7209(11), Fe(1)−N(2) 2.1287(9), P(1)−Fe(1)−P(2) 159.677(12), N(1)−Fe(1)−C(1) 171.851(4).

formanilide (2 equiv with respect to **1**) was introduced into one of the tubes before both samples were exposed to 4 atm H_2. ^{31}P and ^{1}H NMR spectra obtained immediately after H_2 addition displayed resonances for different iron species in each sample. The NMR tube containing formanilide exhibited clean formation of **2**, while the sample without formanilide produced two isomers of the previously reported iron(II) dihydride carbonyl complex ($^{iPr}PN^{H}P$)FeH_2CO (**3**). Heating the samples at 50 °C for 24 h resulted in incomplete catalytic hydrogenation of *N*-methylformanilide to methanol and *N*-methylaniline in both reactions, though the identity of the primary organometallic species remained unchanged. This suggests that the resting states are different in the two catalytic systems and that the primary influence of formanilide is to change the resting state (Figure 8). It is feasible that formation of the relatively stable complex **2** protects the iron from deleterious side reactions during preparation of the catalytic experiment. Additional mechanistic investigations will be required to fully elucidate the influences of formanilide on the catalytic deaminative hydrogenation.

The enhancement of tertiary amide hydrogenation upon addition of formanilide motivated a systematic examination of additive influences, with our focus drawn to dimethylformamide (DMF). DMF was the only formamide substrate from our initial screening (Table 2) that failed to produce any turnover. This is presumably due to the electron-donating nature of the methyl substituents on nitrogen. In addition, DMF hydrogenation is a prominent component in the net hydrogenation of CO_2 to methanol with related ruthenium catalysts.[7e] Prior work in our laboratories has shown significant enhancements in hydrogenation reactions catalyzed by **1** in the presence of Lewis acidic salts, such as lithium triflate (LiOTf), and thus, a set of comparative catalytic experiments on DMF hydrogenation were conducted to ascertain the effect of Lewis acid here (Table 3).

Table 3. Influence of LiOTf and Formanilide on the 1-Catalyzed Hydrogenation of DMF[a]



	additive		
entry	LiOTf	HCON(H)Ph	TON[b]
1	–	–	50
2	0.1 mmol	–	220
3	–	0.1 mmol	190
4	0.1 mmol	0.1 mmol	340

[a]Reaction conditions: 60 atm H_2 (~900 psi), 5.0 μmol of **1** (0.07 mol %), and 7 mmol of DMF in 5 mL of THF at 120 °C for 16 h. [b]Determined by NMR and GC-FID analyses of the product alcohol and residual starting material. Each entry is the average of two or more trials.

DMF hydrogenation experiments in the presence of LiOTf resulted in a significant enhancement of the TON from 50 with no additive (entry 1) to 220 with a 0.1 mmol (1.4 mol %) loading of Lewis acid (entry 2). This increase in activity is comparable to the enhancement obtained by addition of an

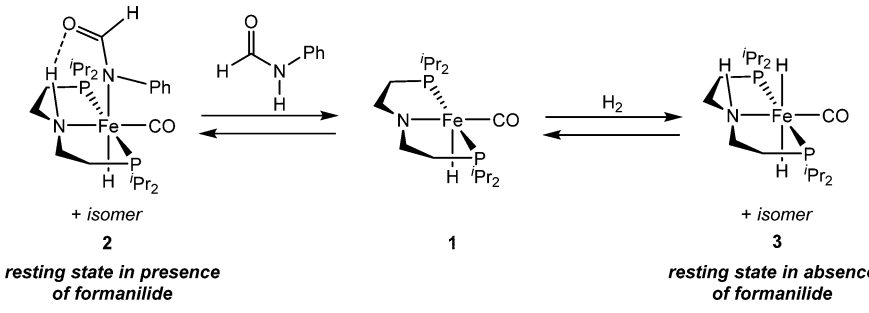


Figure 8. Alteration of the catalyst resting state by formanilide.

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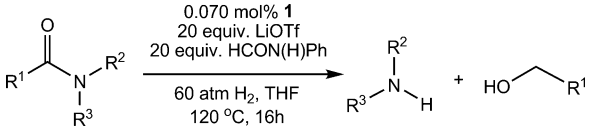
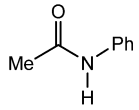
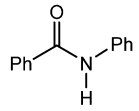
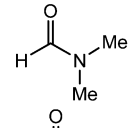
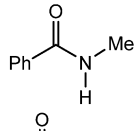
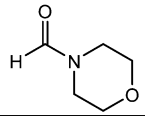
equal amount of formanilide (entry 3), which afforded a TON of 190. A combination of both promotors in an equal molar ratio produced a nearly additive enhancement effect, achieving a TON of 340 (entry 4).

The beneficial influence of both formanilide and LiOTf on the hydrogenation of DMF motivated a brief re-examination of some challenging substrates from Table 2. A selection of amide substrates that achieved low TONs under the prior conditions were evaluated for deaminative hydrogenation by **1** in the presence of both promoters (Table 4). The enhancement of 4-formylmorpholine was also measured for comparative purposes. Addition of 20 equiv of LiOTf and fomanilide (with respect to **1**), along with increasing the temperature and the pressure of H_2, increased the TON for acetanilide and benzanilide from 50 and 130 (Table 2, entries 9 and 10) to 200 and 190, respectively (Table 4, entries 1 and 2). However, the addition of cocatalysts was still unable to produce effective reduction of *N*-methylbenzamide (Table 4, entry 4), likely because of the combination of the sterically demanding arene substituent on the carbonyl and the electron-donating *N*-methyl group. Some enhancement in TON was observed for the already activated substrate 4-formylmorpholine, for which the TON increased from 2000 to 3010 (Table 4, entry 5) under the modified reaction conditions.

Table 4. Hydrogenation of Selected Amides under the Modified Reaction Conditions[a]



Entry	Substrate	TON[b]
1		200
2		190
3		340
4		No conversion
5		3010[c]

[a]Reaction conditions: 60 atm H_2 (900 psi), 5 μmol of **1** (0.070 mol %), and 7 mmol of DMF in 5 mL of THF at 120 °C for 16 h. [b]Determined by GC analysis of the product amine as well as the residual starting material. Each entry is the average of two or more trials. [c]The reaction was conducted with 1.25 μmol of **1** (0.018 mol %).

CONCLUDING REMARKS

The base-free catalytic reduction of amides to amines and primary alcohols by **1** is one of the first observed using a well-defined iron system, and with TONs in excess of 1000 for several substrates, it is superior in activity to most reported ruthenium catalysts. The substrate scope of deaminative amide hydrogenation shows a clear preference for electron-poor amides, possibly originating from an enhanced electrophilicity at the carbonyl and relatively facile delivery of hydride from the iron. Likewise, the substrate scope reveals a preference for sterically unencumbered amides, with even small acetamides and benzamides exhibiting reduced activities compared with the corresponding formamides. Stoichiometric and in situ catalytic NMR studies revealed a difference between iron-catalyzed hydrogenation of secondary and tertiary amides. Secondary amides, and formanilide in particular, rapidly add across the Fe–N bond of **1** to generate the relatively stable Fe–formanilide complex **2**. Complex **2** appears to be the catalytic resting state for hydrogenation reactions conducted in the presence of secondary amides (even when only present in small amounts), while the previously reported Fe–dihydride complex **3** was the primary iron species observed in the hydrogenation of pure tertiary amides. The substantial enhancements in the hydrogenation of tertiary amides in the presence of a small amount of secondary amide likely derive from this change in resting states. However, a more complete mechanistic study, including computational and experimental probes, will be required to fully elucidate the origins of the secondary amide effect as well as enhancements observed by the addition of LiOTf. These investigations as well as further application of the iron-catalyzed methodology are among the foci of our ongoing current work.

EXPERIMENTAL SECTION

General Considerations. All manipulations were carried out using standard vacuum, Schlenk, cannula, or glovebox techniques. Hydrogen was purchased from Airgas and used as received. Catalyst **1** was prepared as previously described.[12h] Amide substrates that were not commercially available were prepared using a previously reported procedure.[15] All other chemicals were purchased from Aldrich, Fisher, VWR, Strem, or Cambridge Isotope Laboratories. Amide substrates were dried and purified by a combination of sublimation and recrystallization from anhydrous ethereal solvents. All other non-volatile solids were dried under vacuum at 50 °C overnight. Solvents were dried and deoxygenated using literature procedures.[16] ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on Bruker 300 MHz DRX, 500 MHz DRX, or 600 MHz spectrometers at ambient temperature, unless otherwise noted. ^{1}H and ^{13}C chemical shifts are referenced to residual solvent signals; ^{31}P chemical shifts are referenced to an external standard of H_3PO_4. Probe temperatures were calibrated using ethylene glycol and methanol as previously described.[17] High-pressure catalytic hydrogenation reactions were performed using a Parr 5500 series compact reactor with glass insert.

Synthesis of (^{iPr}PN^{H}P)Fe(NPhCHO)CO(H) (2). A 20 mL scintillation vial was charged with a sample of **1** (0.050 g, 0.128 mmol) and approximately 5 mL of THF. While stirring, a formanilide solution (0.141 mL of 1 M solution in THF) was added, immediately producing a color change from reddish purple to yellow. This reaction mixture was stirred for 4 h, and then the volatiles were removed under reduced pressure to afford an oily residue. The residue was extracted with pentane (3 mL × 3), filtered through Celite, and evaporated under reduced pressure. The product was recrystallized from minimal pentane at −35 °C overnight to yield **2** (0.041 g, 63%) as a yellow crystalline solid. Crystals suitable for X-ray diffraction were grown by slow evaporation of a pentane solution. Evidence for the purity of **2** is provided by the spectroscopic data in the Supporting Information. ^{1}H NMR (C_6D_6) (two isomers observed): *major isomer*: δ 10.75 (s, 1H, N-*H*), 8.98 (s, 1H, *H*CO), 7.43 (d, 2H, Ph*H*), 7.25 (t, 2H, Ph*H*) 6.96 (t, 1H, Ph*H*), 2.85 (m, 2H, C*H*$_2$), 2.26 (m, 2H, C*H*$_2$), 1.96 (m, 2H,

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CH_2), 1.70 (m, 2H, CH_2), (m, 2H, CH_2), 0.88−1.22 (P^iPr_2), −22.82 (t, J = 57 Hz, Fe-H); *minor isomer*: 10.35 (s, 1H, N-H), 8.81 (s, 1H, HCO), (PhH, CH_2, P^iPr_2 peaks all overlap with those of the major isomer, as confirmed by HMQC NMR spectra), −25.98 (t, J = 51 Hz, Fe-H). $^{31}P\{^1H\}$ NMR (C_6D_6): *minor isomer*: δ 96.85 (d, J = 45 Hz); *major isomer*: 91.14 (t, J = 18 Hz). Partial $^{13}C\{^1H\}$ from HMQC for both isomers: δ 177.08 (HC(O)), 128.49 (Ar), 127.72 (Ar), 122.71(Ar), 53.93, 53.39, 29.43, 28.94, 26.13, 21.11, 24.55, 19.97, 19.74, 19.48 (CH_2 and P^iPr_2).

General Method for Catalytic Amide Hydrogenation Studies. Inside a glovebox, a glass reactor liner (50 mL) was charged with the amide (7 mmol) and THF to a total volume of 5 mL. Then a solution of **1** (either 5.0 or 1.25 μmol) in THF was added to this mixture via microsyringe. If LiOTf, formanilide, or other additives were tested, they were added at this time. Then the Parr reactor was sealed and removed from the glovebox. The reactor was pressurized with commercial-grade H_2 at ambient temperature (~450 or 900 psi) and then heated (100 or 120 °C in typical experiments) with mechanical stirring. After the allotted time (4−16 h), the reactor was cooled by submersion in an ice bath, and the H_2 was slowly vented. The product solution was then analyzed by ^1H NMR spectroscopy and GC-MS or GC-FID using mesitylene as a standard.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.6b00816.

Crystallographic data for **2** (CIF)
Additional experimental data and selected NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: bernskoetterwh@missouri.edu.

Notes

The authors declare no competing financial interest.

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